## REMARKS

### I. THE AMENDMENTS

After entry of this Amendment Claims 29-48 are pending in this Application. Applicants have canceled Claims 1-28 without prejudice. Applicants reserve the right to pursue the subject matter of Claims 1-28 in another related application. Applicants added new Claims 29-48 to replace the canceled claims in order to further define the invention. The new claims are supported throughout the specification. Specifically, new Claim 29 is supported on page 3, line 32; on page 6, line 7, and on page 7, line 20. Claims 30, 31, 34 and 35 are supported on page 13, line 36. Claims 32 and 36 are supported on page 13, line 27. Claim 33 is supported on page 16, lines 12-13. Claim 37 is supported on page 14, line 1. Claim 41 is supported on page 10, line 34 and on page 14, line 1. Claims 38-40 and 42-44 are supported on page 16, line 23. Claims 45-48 are supported on page 14, line 5. No new matter has been introduced by the new claims.

The specification has been amended to insert sequence identifiers in accordance with the sequence rules. No new matter has been added.

### II. INFORMALITIES

***Drawings.*** The Applicants will submit formal drawings once a Notice of Allowance has been issued.

***Specification.*** The specification is objected to for failing to comply with the requirements of 37 C.F.R. §§ 1.821 through 1.825. Tables 1 and 2 are objected to by the Examiner as not being a part of the specification. The Examiner suggests that Tables 1 and 2

be canceled and replaced with identical tables to be inserted into the specification. The Applicants have amended the specification to refer to specific SEQ ID NOS and Tables 1 and 2 have been incorporated into the specification as page numbers 30-37.

***Claims.*** Claims 1-11 and 26-27 are objected to for failing to recite SEQ ID NOS. The Applicants have canceled Claims 1-11 and 26-27 without prejudice, and replaced them with new Claims 29-48 which recite SEQ ID NOS.

## III. THE INVENTION

The Applicants have identified and characterized about 235,000 base pairs of genomic DNA corresponding to the Hereditary Hemochromatosis gene ("HH gene") and surrounding sequences. By comparing this sequence between an HH affected individual and an unaffected individual, numerous polymorphisms throughout the sequence were identified that distinguished an HH affected individual from an unaffected individual. Using such sequence data, the Applicants have devised nucleotide molecules for the diagnosis of hemochromatosis.

## IV. THE REJECTIONS

### A. The Rejections Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1-11 and 26-27 are rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention as claimed. In particular, the Examiner states that "the specification, while being enabling for oligonulceotides consisting of at least 8 to about 100 consecutive bases which would contain

a specified polymorphism, does not reasonably provide enablement for oligonucleotides comprising at least 8 to about 100 consecutive bases containing a polymorphic site." *See*, paper No. 10, page 4. According to the Examiner, "[t]he specification does not teach the specificity of the polymorphisms for being within the sequences of SEQ ID NOS:1 and 2 and said sequences, particularly those which are short sequences, may also be present in unrelated genomic sequences or usable as probes/markers for unrelated mutations and/or conditions." *See*, paper No. 10, page 4.

Claims 1-11 and 26-27 have been canceled with entry of this Amendment, thus obviating those rejections. The Applicants will address the enablement of new Claims 29-48 below.

***The Legal Standard.*** The legal standard for enablement under 35 U.S.C. §112 requires that "'[...] a patent specification must disclose sufficient information to enable *those skilled in the art* to make and use the claimed invention.'" (emphasis added) *Hormone Research Foundation, Inc. v. Genentech*, 15 USPQ2d 1039, 1047 (Fed. Cir. 1990). "Enablement is not precluded by the necessity of some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" *In re Wands*, 858 F.2d 731, 736-737 (Fed. Cir. 1988). Furthermore, "the fact that experimentation may be complex . . . does not necessarily make it undue, if the art typically engages in such experimentation." *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (U.S. Intl. Trade Comm. 1983). With regard to the necessary teaching in light of the knowledge and skill possessed by the skilled artisan, the Federal Circuit held that "a patent need not teach,

and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81 (Fed. Cir. 1986). Finally, "[t]he enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engel Industries, Inc. v. Lockformer Co.*, 946 F.2d 1528, 1533 (Fed. Cir. 1991).

***New Claims 29-48.*** The new claims recite an "isolated, extrachromosomal polynucleotide" and further refer to SEQ ID NOS:1 and 2. Claims 29-48 are fully enabled in the disclosure of the pending application. Figures 1 (SEQ ID NO:1) and 2 (SEQ ID NO:2) provide about 235,000 bases of nucleotide sequence including and surrounding the HH gene. Tables 1 and 2 provide examples of polymorphic sites along this sequence that can be used for diagnostic purposes. For example, Table 1 "provides 397 new polymorphic sites in the region of the HH gene." *See*, page 11, line 25. In addition, Table 2 lists the frequency of about 100 of the alleles defined by the polymorphic sites of the invention in the general population. *See*, page 12, line 21. The specification further provides general teaching regarding methods of using such information to diagnose and detect haemochromatosis (*e.g.*, page 6, lines 20-26 and page 16, line 21 through page 18, line 23). Also provided is disclosure on screening (*e.g.*, page 14, line 9 through page 16, line 19), expression of polynucleotides (*e.g.*, page 18, line 25 through page 23, line 3), purification of proteins (*e.g.*, page 23, lines 5-26), antibodies (*e.g.*, page 23, line 28 through page 24, line 17).

The Applicants respectfully submit that "the description enables any mode of making and using the claimed invention." *Engel Industries, supra.* Thus, the subject invention is

fully enabled under the applicable standard for enablement as enunciated by the Federal Circuit[1].

***In re Fisher.*** The Examiner cites *In re Fisher*, 166 USPQ 18 (CCPA 1970) for the proposition that in "the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute." *See*, paper No. 10, page 4. The Applicants respectfully submit that the Examiner misapplies *In re Fisher* to the presently claimed invention.

The claims at issue in *In re Fisher* covered an "adrenocorticotrophic hormone preparation containing at least 1 International Unit of ACTH per milligram ... further characterized as containing ... [a] polypeptide of at least 24 amino acids having" a sequence recited in the claim. *Id.* at 20. The court found in the disclosure a "lack of teaching of how to obtain other-than-39 amino acid ACTHs", *id.* at 23, and a "problem arising from the potency recitation[.]" *Id.* at 23.

The present case is distinguishable from *In re Fisher*. The Applicants have disclosed detailed information regarding the sequence of and surrounding the HH gene, polymorphic sites contained in this sequence, the frequency of polymorphic sites in the population and the use of the disclosed polymorphisms to diagnose HH. The specification also teaches polynucleotides containing a sequence as described in Figure 1 or 2. The specification also teaches the incorporation of the described polynucleotides into vectors. Such a vector

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[1] The disclosure of a biotechnology patent "is not directed to a layman, but rather to a person having ordinary skill in the art, versed in the field of molecular biology and the use of recombinant DNA techniques. That hypothetical person is presumed to be familiar with technology and techniques in the field of cloning at the time the invention was made[.]" *Ex parte Goldgaber*, 41 USPQ2d 1172, 1174 (BPAI 1996).

construct is clearly enabled and "based ... on" the teachings of the Applicants, *see, In re Fisher*, at 24.

Furthermore, the application which was at issue in *In re Fisher* was filed in 1960 with a priority date in 1949, *id.* at 19-20, whereas the pending application was filed in 1997 with a priority date in 1996. Thus, the present application has to be evaluated based on its own disclosure and the state of the art, not that in *In re Fisher*, and it has to be evaluated based on what is known by a skilled artisan in the area of "physiological activity" about 47 years after *In re Fisher. See also, Ex parte Goldgaber, supra.*

In view of the above, the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

**B. The Rejections Under 35 U.S.C. § 101 Should Be Withdrawn**

Claims 1-11 are rejected under 35 U.S.C. § 101 on the grounds that the claimed invention is directed to non-statutory subject matter. In that regard, the Examiner states that "the claims ... broadly read upon a human being, which is a product of nature and constitutes non-statutory subject matter." *See*, paper No. 10, page 5.

Claims 1-11 have been canceled with entry of this Amendment, thus obviating those rejections. New Claims 29-48 have been added. Claims 29-48 recite an "isolated, extrachromosomal polynucleotide". Thus, new Claims 29-48 do not read on a human being or a product of nature, and are therefore directed to patentable subject matter under Section 101.

In view of the above, the rejections under 35 U.S.C. § 101 should be withdrawn.

## C. The Rejections Under 35 U.S.C. §102(b) Should Be Withdrawn

Claims 1-11 and 26-27 are rejected under 35 U.S.C. §102(b) on the grounds that they are anticipated by Vogel *et al.*, *Human Chromosomes, in* Human Genetics, 18-81 (Vogel *et al.* eds., 1982) ("Vogel"). According to the Examiner, Vogel "teaches isolated human chromosomes (Figures 2.9 and 2.10 in particular), including chromosome 6, from which the sequence of Figures 1 and 2 are ultimately derived." See, paper No. 10, pages 5-6. The Applicants respectfully disagree.

Claims 1-11 and 26-27 have been canceled with entry of this Amendment, thus obviating those rejections. The Applicants will address the novelty of new Claims 29-48 in view of Vogel below.

***The Legal Standard.*** For a rejection based on anticipation under 35 U.S.C. § 102, the Examiner must show "that all of the elements and limitations of the claim are found within a single prior art reference." *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991). A finding of anticipation is only proper in case of a "single prior art disclosure of all elements of a claimed invention arranged as in the claim." *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983).

The level of disclosure required for a reference under 35 U.S.C. § 102 (b) was pronounced by the court in *In re Sasse*, 207 USPQ 107, 111 (CCPA 1980):

> ... the proper test of a description in a publication as a bar to a patent as the clause is used in section 102 (b) requires a determination of whether one skilled in the art to which the invention pertains could take the description of the invention in the printed publication and combine it with his own knowledge of the particular art and from this combination *be put in possession of the invention on which a patent is sought.* Unless this condition prevails, the description in the printed publication

is inadequate as a statutory bar to patentability under section 102 (b).

*Id.* at 111 (citations omitted, emphasis in original).

Thus, a proper reference under Section 102 "must exhibit a substantial representation of the invention in such full, clear, and exact terms that one skilled in the art may make, construct and practice the invention without having to depend on either the patent or on his own inventive skills." *Philips Electronics Corp. v. Thermal Industries, Inc.*, 171 USPQ 641, 644 (3d Cir. 1971).

***The Vogel Reference.*** As discussed, *supra*, the new claims recite an "isolated, extrachromosomal polynucleotide" and further refer to SEQ ID NOS:1 and 2. The Vogel reference discloses the "Preparation and Staining of Mitotic Metaphase Chromosomes", *see*, Vogel, page 23. Vogel states that "[t]o obtain preparations in which the chromosomes are spread out in one plane, the cells are treated for a short time (10-30 min) with a hypotonic solution. The cells are then fixed with ethanol and acetic acid, a drop of the cell suspension is placed on the slide, air-dried, and stained." *See*, Vogel, page 23. Then, the Vogel reference goes on to discuss staining methods, page 23, and banding methods (i.e., staining to visualize "density differences" and thus bands along the chromosomes), page 24.

However, nowhere does the Vogel reference discuss the "isolation" of a chromosome. The "preparations" of chromosomes as disclosed in Vogel involve that "cells are fixed ... placed on [a] ... slide, air-dried, and stained", yet, nowhere in the process discussed in Vogel are the chromosomes "isolated". In the process discussed in Vogel, chromosomes are

"stained", *i.e.*, made distinguishable from the remaining components of the cells in order to facilitate their identification[2].

Figures 2.9 and 2.10, referred to by the Examiner, are discussed in the Vogel reference on page 24 in a subsection entitled "Banding Techniques." *See*, Vogel, Figure 2.9, page 26 shows a "[k]aryotype of a human male stained conventionally and using different banding techniques", and Figure 2.10, page 28, shows a "[k]aryotype of a human male; Q (*right*) and R (*left*) banding." (Emphasis in original.) However, the karyograms presented in Figures 2.9 and 2.10 in Vogel were only used to exemplify the staining techniques discussed before, *supra*. The chromosomes were merely rendered more visible for identification in Figures 2.9 and 2.10, but they were not "isolated", as suggested by the Examiner.

Thus, "one skilled in the art [of biotechnology] ... could [not] take the description of [the Vogel reference] ... and combine it with his own knowledge ... and from this combination *be put in possession of the invention*" as taught in the pending application. *In re Sasse, supra.*

Moreover, the Vogel reference does also not render the pending claims obvious as it does not suggest the subject matter of Claims 29-48 with a reasonable expectation of success.

In view of the above, the rejections under 35 U.S.C. § 102 (b) should be withdrawn.

**D. <u>Rejections Under 35 U.S.C. §§ 102(b)/103(a) Should Be Withdrawn</u>**

Claims 1-11 and 26-27 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Boretto *et al.*, 1992, Hum.

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[2] For example, the Vogel reference discusses "Electron-Microscopic Pictures from Human Chromosomes", at page 31, and describes "[t]hree types of fibrils ... [the] third only 30-50 Å" in diameter. The third fibril, according to Vogel, "corresponds to a DNA fiber together with proteins (histone and nonhistone)." *See*, Vogel, at 31.

Genet. 89:33-36 ("Boretto"). The Examiner relies on *In re Best*, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922 (BPAI 1989) in rendering this rejection based on inherency under 35 U.S.C. §102(b) and obviousness under 35 U.S.C. §103(a).

According to the Examiner, Boretto "teaches anonymous markers and polymorphic sites on human chromosome 6 which identify human hemochromatosis. ... The oligonucleotides of the claimed invention and the markers taught by Boretto et al appear to be the same or similar absent a showing of unobvious differences." *See*, paper No. 10, pages 6-7. Furthermore, according to the Examiner, "[i]n the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from those taught by the prior art and to establish patentable differences." *See*, paper No. 10, page 7. The Applicants respectfully disagree.

Claims 1-11 and 26-27 have been canceled with entry of this Amendment, thus obviating those rejections. The Applicants will address the novelty of new Claims 29-48 in view of Boretto below.

**a. <u>Claims 29-48 Are Not Inherently Anticipated</u>**

***The Legal Standard.*** In order to find anticipation through inherency, "evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. USA Inc. v. Monsanto Co.*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Inherency, thus, applies "where the common knowledge of technologists is not recorded in the reference; that is, where technological facts are known to those in the field of the invention, albeit not known to judges." *Continental Can*, at 1749-50. Yet, "[i]nherency ... may not be established

by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *Continental Can*, at 1749 (citations omitted, emphasis in original).

***The Boretto Reference.*** Boretto discusses "[a]nonymous markers located on chromosome 6 in the HLA-A class I region", *see*, Boretto, page 33. However, Boretto does not describe any nucleotide sequence, hence, "*anonymous* markers". The "[a]llelic distribution of the anonymous markers was ... studied", *see*, Boretto, page 33. "The results [presented in Boretto] suggest **two** possible locations for the haemochromatosis gene: less than 100 kb centromeric to the HLA-A locus, or on the telomeric side."[3] *See*, Boretto, page 33 (emphasis added).

Instructive is Figure 2 in Boretto, page 35, especially when examined in combination with the results presented in Table 1, page 35. Figure 2 shows a "[s]chematic structure of the HLA-A class I region and localization of ... loci" corresponding to four different markers[4]. *See*, Boretto, page 35. In Table 1 the "strength of association between [normal and haemochromatosis] alleles are given by Yule's association coefficient A" for the four different markers, *see*, Boretto, page 34. Table 1 indicates "two significant differences", *see*, Boretto, page 35, of marker-association with patients and controls, the markers P3(B) and i82 are significantly more associated with patient alleles than with control alleles. *See*, Boretto, page 35.

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[3] Thus, Boretto does not "describe the applicant's claimed invention sufficiently to have placed a person of ordinary skill in the field of the invention in possession of it." *In re Spada*, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990).

[4] The P3 marker identified two different loci, named P3A and P3B. See, Boretto, page 34.

However, these results of marker-association presented in Boretto are inconclusive for purposes of determining the location of the hemochromatosis gene. The reasons are at least two-fold. First, the two loci that show a "significant difference[]" are located at significant distances on the chromosome, compelling the authors to conclude that there are "two possible locations for the haemochromatosis gene", *see*, Boretto, page 33. Second, one locus (*i.e.*, the i97 locus) was found "less than 50 kb" from the locus with the highest "Yule's association coefficient A" and between both loci with the "two significant differences", *see*, Boretto, page 35. Yet, the i97 locus did **not** show a significant difference in association between patients and controls. Thus, the Boretto reference could only conclude that "the haemochromatosis gene is either less than 100 kb centromeric to HLA-A, or telomeric to HLA-A and possibly very close." *See*, Boretto, page 36. Furthermore, Boretto cautions that "[s]ince there is not always a direct link between association and physical distance, and indeed sometimes the two are in complete contradiction, we must remain cautious in our interpretation of the results ...." *See*, Boretto, page 36.

Thus, contrary to Federal Circuit precedent on inherency, "the missing descriptive matter is [**not**] necessarily present in the thing [,*i.e.*, nucleotides,] described in the [Boretto] reference", *Continental Can, supra.* In other words, Boretto is not merely missing "common knowledge of technologists [that is] ... known to those in the field of the invention, albeit not known to judges." *Continental Can, supra.* In fact, the clear statement in Boretto that "the haemochromatosis gene is either less than 100 kb centromeric to ..., or telomeric to ... and possibly very close" to a locus on the chromosome exemplifies the "probabilities or

possibilities" through which "[i]nherency ... may not be established", *Continental Can, supra*[5].

***In re Best.*** The Examiner cites *In re Best*, 195 USPQ 430 (CCPA 1977) in support of the proposition that the "the burden is on the Applicant to prove that the claimed materials are different from those taught by" Boretto, *see*, paper No. 10, page 7. Yet, *In re Best* does not support a shifting of the burden of proof in view of a reference that is as deficient as Boretto.

In *In re Best*, the claimed invention covered crystalline zeolitic aluminosilicate which was defined by two molar ratios (*i.e.*, $SiO_2/Al_2O_3$ and $Na_2O/Al_2O_3$) and four other parameters (*i.e.*, the cubic unit cell size, the ion exchange capacity, the oxygen adsorption capacity, and the X-ray powder diffraction pattern). *Id.* at 434. The two molar ratios disclosed in one prior art reference, Hansford, were within the range of those in the claimed invention, yet, the other parameters were not specifically disclosed in Hansford. *Id.* at 434. The applicants in *In re Best* claimed that the other parameters were the result of their claimed process. *Id.* at 434. However, the products of the claimed invention and Hansford were "produced by identical or substantially identical processes." *Id.* at 433. Therefore, the court held that an applicant could be asked "to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product." *Id.* at 433.

The pending case is clearly distinct. According to the Examiner, "the markers taught by Boretto et al appear to be the same or similar" to the nucleic acids taught by the Appliants. The court in In re Best, however, qualified its holding by saying that "[w]here ... the claimed

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[5] Indeed, the Boretto reference is deficient as it "offers no more than a starting point for further experiments, [as] ... its teaching will sometimes succeed and sometimes fail, [and] ... it does not inform the art ... how to practice the invention, [thus,] it has not correspondingly enriched the store of common knowledge[.]" *Dewey & Almy Chemical Co. v. Mimex Co., Inc.*, 52 USPQ 138, 142 (2d Cir 1942).

and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes", *id.* at 433. Neither scenario applies in the pending case, *i.e.*, the "products are [not] identical or substantially identical" and the products "are [not] produced by identical or substantially identical processes". In other words, unlike in *In re Best*, the Applicants do not rely on parameters they decided to determine but that happen not to be specifically disclosed in the Boretto reference.

In the pending examination, the reference cited by the Examiner, Boretto, clearly states that "the haemochromatosis gene is either less than 100 kb centromeric to ..., or telomeric to ... and possibly very close" to a locus on the chromosome. Thus, an "identical or substantially identical" product or process that could possibly make the pending application fall under *In re Best* has not been established.

***Ex parte Gray.*** The Examiner also cites *Ex parte Gray*, 10 USPQ2d 1922 (BPAI 1989) in support of the proposition that the "the burden is on the Applicant to prove that the claimed materials are different from those taught by" Boretto, *see*, paper No. 10, page 7. Yet, also *Ex parte Gray* does not support a shifting of the burden of proof in view of a reference that is as deficient as Boretto.

The applicants in *Ex parte Gray* sought protection for "human nerve growth factor β-NGF, identified by the particular amino acid sequence and being free from other proteins of human origin (claim 1)." *Id.* at 1923. Two references were asserted, entitled "'Isolation of Human Nerve Growth Factor From Placental Tissue,'" and "'Human Nerve Growth Factor: Lack of Immunocrossreactivity with Mouse Nerve Growth Factor,'" *id.* at 1923. The Board

in *Ex parte Gray* concluded that "the difference between the material of Goldstein and of Walker [,*i.e.*, the two asserted references,] and that claimed by appellants herein resides in the method of obtaining the human growth factor. The prior art material is recovered from natural sources and purified, while appellants' is produced by recombinant DNA methodology." *Id.* at 1924.

Thus, unlike the Boretto reference which "debates"[6] the hemochromatosis gene in nebulous "either-or-and-possibly" terms, the two references in *Ex parte Gray* unambiguously proclaim the "[i]solation of" the composition sought to be patented by the *Ex parte Gray* applicants. Thus, the pending case does not fall under *Ex parte Gray* either.

In view of the above, the rejections under 35 U.S.C. § 102 (b) should be withdrawn.

**b. Claims 29-48 Are Not Obvious**

***The Legal Standard.*** For a rejection based on obviousness under 35 U.S.C. § 103, the Federal Circuit has pronounced a two factor test which asks

> (1) whether the *prior art would have suggested* to those of ordinary skill in the art that they should *make the claimed composition or device, or carry out the claimed process*; and (2) whether the *prior art would also have revealed* that in so making or carrying out, those of ordinary skill would have a *reasonable expectation of success*.

*In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991) (emphasis added).

The *In re Vaeck* court explained that "[b]oth the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *Id.* at 493.

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[6] Again, the Boretto reference at best suggests places where one might look for the hemochromatosis gene, yet, it clearly concedes its own failure of actually locating it.

In *In re Eli Lilly & Co.*, 14 USPQ2d 1741 (Fed. Cir. 1990) the Federal Circuit espoused a test for the "discredited 'obvious-to-try' category of disclosure", *id.* at 1743. According to In re Eli Lilly & Co.,

> [a]n 'obvious-to-try' situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of *how to obtain the desired result*, **or** that the claimed *result would be obtained if certain directions were pursued.*

*Id.* at 1743 (emphasis added).

Finally, "[i]nherency and obviousness are distinct concepts." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ2d 303, 314 (Fed. Cir. 1983). "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *In re Spormann*, 150 USPQ 449, 452 (CCPA 1966). Thus, "a retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." *In re Newell*, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989).

***The Boretto reference.*** As discussed above, the Boretto reference discusses a failed attempt at isolating the hemochromatosis gene. Thus, Boretto falls far short of providing a suggestion for the hemochromatosis gene described in the pending application and it falls far short of providing an expectation of success in obtaining the hemochromatosis gene. Moreover, the Boretto reference falls squarely into the defunct obvious-to-try category of references. First, Boretto "does not contain a sufficient teaching of how to obtain the" hemochromatosis gene. *In re Eli Lilly & Co., supra.* Second, Boretto does not teach "that the

[hemochromatosis gene] ... would be obtained if certain directions were pursued." *In re Eli Lilly & Co., supra.*

The pending rejections are similar to an obviousness challenge dismissed in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). In *Amgen*, claims to the human EPO gene were challenged as obvious over a sequence probe specific for the monkey gene that was available in the art and that could have been used to screen a library for the human gene. *Id.* at 1022-1023. Affirming the district court, the Federal Circuit in *Amgen* held that

> [w]hile the idea of using the monkey gene to probe for a homologous human gene may have been obvious to try, the realization of that idea would not have been obvious. There were many pitfalls. Hindsight is not a justifiable basis on which to find that ultimate achievement of a long sought and difficult scientific goal was obvious.

*Id.* at 1023.

The Boretto reference itself shows that the isolation of the hemochromatosis gene is nonobvious. First, the Boretto reference does not report the finding of the gene. Second, the Boretto reference states that the authors of the reference "have been working[] since 1988" trying to isolate the hemochromatosis gene, yet, without success.

In view of the above, the rejections under 35 U.S.C. § 103 (a) should be withdrawn.

## CONCLUSION

In view of the foregoing amendments and remarks, the Applicants believe that the application is in good and proper condition for allowance. Early notification to that effect is earnestly solicited. If the Examiner feels that a telephone call would expedite the consideration of the application, the Examiner is invited to call the undersigned attorney at (212) 790-9090. The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 16-1150 for any matter in connection with this response, including fees for the extension of time, which may be required. A copy of this sheet is enclosed.

Respectfully submitted,

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